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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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FISH & RICHARDSON P.C.
P.O BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
12/17/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/587,633	ALCARAZ ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-55* is/are pending in the application.

4a) Of the above claim(s) *31-33, 35, 37 (2nd), 38-39, 45-53, 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-16, 18-27, 28-30, 34, 36-37 (1st), 40-44, 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/28/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group II, claims 28-30, 34, 40-44, 54 and claims 15-16, 18-27, 36-37 (1st) reading on R3 is thiazolyl, oxazolyl, triazolyl or tetrzolyl in the reply filed on Aug. 10, 2009 is acknowledged.

Claims 31-33, 35, 37 (2nd), 38-39, 45-53, 55 and the remaining subject matter of claims 15-16, 18-27, 36-37 (1st) are withdrawn from consideration per 37 CFR 1.142(b).

2. Claims 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as well as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention or as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916), where the Supreme Court looked to whether the experimentation needed to practice an invention was undue or unreasonable. *Id*. An invention must be described so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". The analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *Id*. at 740, *Id*. at 1407. The factors to be considered herein are those set forth as the In re Wands, 8 USPQ 2nd 1400 (1988) decision.

The analysis is applied to the instant case.

Nature of invention

The claims are drawn to compounds which have chemokine receptor inhibiting activity including compounds of formula I, and solvates and solvates of salt thereof.

Breadth of the claims

The scope of the claims included enormous number of compounds, pharmaceutically acceptable acid or base addition salts and *solvates and solvates of salt thereof.*

The state of the art

Chemokine receptors exist in multiple subtypes with different locations of expression and therefore different functions (Rollins BJ. Blood. 1997, 90(3): 909-928 ; page 910, Table 1; page 912, Table 2). While many diseases are implicated to be mediated by the chemokine receptors, the particular responses elicited by each subtype have not been delineated (page 920, Conclusion). The level of the skilled in the chemokine receptor art is high because after 10 years of intensive research, still very little understanding can be made (see p. 920 conclusion). There is no predictable structure for such utility.

Predictability/unpredictability of the art.

The high degree of unpredictability is well recognized in the chemokine receptor ligand art. Although some understanding of functionality can be made, however, to date, only limited understanding of mechanisms that lead to one activity over another when a "specific" chemokine is involved (see Cohen CA 125:31527). One of ordinary skill in the art would therefore have little basis to extrapolate the results to compounds structurally removed from the known compounds.

Level of ordinary skill

Unlike formation of salts between a phamceutically acceptable acid and an organic base compound of the claims, the formation of "solvates" must find descriptive and enabling support for such claimed scope. (see Braga et al. p.3640). Absent of what solvent, what kind of solvate was being formed under what condition, it is a nightmare for artisan in the field to make solvates.

Amount of experimentation/guidance

The claims encompassed the scope of "solvates or solvates of the salt of the compounds" for which no description or enabling support can be found in the specification. A survey of the specification indicated there is no description of which solvent can form solvate with the compounds, under what condition will such solvates be obtained, and whether the solvates will have consistent properties to be considered inclusive as being a "Markush" alternative of the compounds.

Working examples

No examples, no process of making, no starting material or operability can be found for any compound encompassed by the Markush formula to have the ability in forming what solvate. Therefore, absent of description and enabling disclosure, the specification is insufficient in supporting the "claimed" scope of "solvates of the compounds or a salt of the compounds".

3. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is very confusing as to the scope of "R^3 is a group having an NH or OH that has a calculated or measured pKa of 1.0 to 8.0". Please note that the R^3 moiety is part of a chemical structure. Such definition of containing NH or OH with a calculated or measure pKa range is unclear as to what is the chemical structure. There is no description as to where a calculated basis can be found such as chemical handbooks etc. or how such measurements are made. There is no data base or chemical text as to what these functional groups are. It is recommended that the specific moieties and substituents be explicitly listed.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 15-16, 18-27, 28-30, 34, 36-37 (1st), 40-44, 54 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2005/0107428 (1449) in view of Kenner or Kasende.

US 2005/0107428 disclosed many compounds wherein the R3 moiety are substituted heterocyclic moieties such as p.72 example 233. If one interpretes the above discussed R3 being any heterocyclic moiety with the required pKa range, then, inherent anticipation would be found. The oxo-pyrimidone is a tautomer of hydroxyl pyrimidone and the pH recited by Kenner or Kasende for oxo-pyrimidone is within the range of the claims. Therefore, merely on the limitation of pKa ranges, the many exemplified compounds of '428 would be inherently anticipating the instant claims.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 15-16, 18-27, 28-30, 34, 36-37 (1st), 40-44, 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alcaraz et al. US 2005/0107428 (recited on 1449) in view of Kenner or Kasende.

Determination of the scope and content of the prior art (MPEP §2141.01)

Alcaraz et al. '428 disclosed analogous compounds wherein the R3 moiety is a heterocyclic group optionally substituted. A particular species is found on p.47 example 40.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the exemplified compound 40 and the elected species is that instead of a thiazolyl ring, the prior art has a pyrazolyl ring, instead of two substituents (CF3 and oxo), the prior art has only CF3 substitution. Generically, it was taught that the R3 moiety (R9 of prior art) being pyrazolyy or thiazolyl is an optional choice for one having ordinary skill (see p.2, [0037]lines 7-8) and the substituents are optionally single or multiple including oxo (seep.1, [0022]).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would be motivated to modify the exemplified compound 40 of prior art with the generic teaching of the reference. The large number of exemplification would provided sufficient enablement that the whole generic description would be expected to have similar utility. The instant claims are mere picking and choosing among the generic disclosure of the prior art with a narrow combination of the genus as described by the prior art. Especially, the picking and choose was motivated by the pKa range for which the prior art although is silent about the pKa, the exemplified species is well within such pKa values (see Kenner or Kasende and example 233). In absence of unexpected results, there is nothing unobvious in choosing some among many. In re Lemin 141 USPQ 814.

6. Claims 15-16, 18-27, 28-30, 34, 36-37 (1st), 40-44, 54 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 10/504,936 or claim 18 of copending Application No. 11/866,611 in view of Kenner or Kasende.

The same rational for finding of obviousness as delineated supra for the 103 rejection is also applicable here and incorporated by reference.

This is a provisional obviousness-type double patenting rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Dec. 3, 2009

/Celia Chang/
Primary Examiner
Art Unit 1625